

CHAPTER 27

Peripheral Lymphadenopathy

KEY TEACHING POINTS

- In patients presenting with peripheral lymphadenopathy lasting several weeks, 18% to 24% will eventually be diagnosed with malignancy and up to 5% will be diagnosed with serious infection.
- In patients with lymphadenopathy, the following findings increase the probability of serious disease: fixed nodes, large nodes ($\geq 9 \text{ cm}^2$), weight loss, supraclavicular adenopathy, and hard nodes.
- The Lymph Node Score (developed by Vassilakopoulos) further refines bedside diagnosis, particularly in the identification of patients unlikely to have serious disease.
- The *ulceroglandular* and *oculoglandular* syndromes are defined by bedside findings. Each syndrome is associated with specific infectious diseases.
- When staging cancer patients, physical examination lacks sufficient sensitivity to reliably exclude metastatic involvement of the lymph nodes.

I. INTRODUCTION

Lymphatic vessels are located in all tissues and organs of the body except the central nervous system. These vessels collect extracellular tissue fluid (or lymph) and carry it to the systemic venous system, traversing along the way regional collections of bean-shaped structures called **lymph nodes**. As these lymph nodes slowly filter the lymph fluid, they may encounter microbes, malignant cells, particulate debris, or other substances to which they react, enlarge, and harden. Should such nodes enlarge or harden enough, they may become palpable, a problem called **peripheral lymphadenopathy**.

Ancient Greek and Roman physicians recognized peripheral lymphadenopathy as an important sign of tuberculosis (scrofula),^{1,2} and for more than a century clinicians have known that lymphadenopathy may signify serious disorders, such as carcinoma, lymphoma, leukemia, and certain infectious diseases (tuberculosis, syphilis, and plague, among others).³ How often adenopathy reflects one of these serious disorders in current practice depends on the clinical setting. In family practice clinics, peripheral lymphadenopathy is benign 99% of the time, sometimes reflecting known disorders (such as pharyngitis, dermatitis, or insect bites) but more often appearing and resolving without explanation.^{4,5} In specialized lymph node clinics, however, 18% to 24% of referred patients are eventually diagnosed with malignancy (i.e., lymphoma or metastatic cancer) and up to 5% have a treatable infectious or granulomatous disorder (e.g., tuberculosis, human immunodeficiency virus [HIV] infection, sarcoidosis).⁶⁻⁸ This chapter focuses on the physical findings that help to discriminate serious causes of lymphadenopathy from more benign causes.

II. ANATOMY AND PATHOGENESIS

A. INTRODUCTION

The lymphatic drainage of the body is subdivided into seven distinct regions, all of which converge and drain into the great veins near the base of the neck (Fig. 27.1). A normal adult has approximately 400 to 450 lymph nodes, although only about a quarter are in locations that could ever become palpable: 30 in the arm and axilla, 20 in the leg, and 60 to 70 in the head and neck (the remaining lymph nodes reside deep in the thorax and abdomen and are detectable only by clinical imaging).⁹ Anatomists divide lymph nodes into superficial nodes and deep nodes, based on whether they accompany superficial or deep blood vessels. Superficial nodes lie just under the surface of the skin, accompany superficial veins, and often are visible when enlarged. Most palpable nodes are superficial nodes. The only deep nodes detectable by bedside examination are the deep cervical nodes (which accompany the carotid artery and internal jugular vein under the sternocleidomastoid muscle) and the axillary nodes (which surround the axillary vessels).

The fact that lymph nodes accompany blood vessels is helpful when searching for two nodal groups: (1) the epitrochlear nodes, which lie near the basilic vein, and (2) the vertical group of inguinal nodes, which surround the proximal saphenous vein (Fig. 27.2).

B. REGIONAL LYMPH NODE GROUPS

Maps of regional lymphatic drainage are based on older experiments in living humans and cadavers, in which injections of mercury, Prussian blue, radiocontrast materials, or other dyes were used to highlight normal lymph channels and regional nodes.⁹⁻¹² (Lymph vessels are otherwise difficult to distinguish from small veins during dissection.) These maps of lymph drainage are helpful because they allow clinicians to predict the spread of local infections or neoplasms and, when faced with isolated adenopathy, to focus the diagnostic search to a particular region. Nonetheless, clinical experience demonstrates that disease does not always spread in an orderly way through these channels and nodes. For example, infections and malignancy may occasionally skip one regional node group to travel to another (e.g., an infection of the ring finger may involve the axillary nodes and skip the epitrochlear nodes), and malignancy may sometimes travel in a retrograde direction between nodal groups (e.g., supraclavicular adenopathy; see the section on [Supraclavicular Nodes](#)).¹¹ In addition, despite the implication of these maps, isolated adenopathy does not necessarily reflect focal disease but instead may represent the sole sign of a generalized disorder (e.g., tuberculosis or lymphoma).

I. CERVICAL NODES

All structures of the head and neck drain into the deep cervical nodes, either directly or via intermediary superficial nodes (Fig. 27.3). The skin of the face and neck drains into the superficial nodes in a predictable fashion (see Fig. 27.3). The pharynx, nasal cavity, and sinuses usually drain to the upper deep cervical nodes; the mouth and teeth to the submandibular nodes and eventually the upper cervical nodes; and the larynx to both upper and lower cervical nodes. The tongue has the most diverse drainage: efferents travel to the submental, submandibular, upper deep cervical, and lower deep cervical nodes, and disease near the midline may travel to either side.^{9,11,13,14}

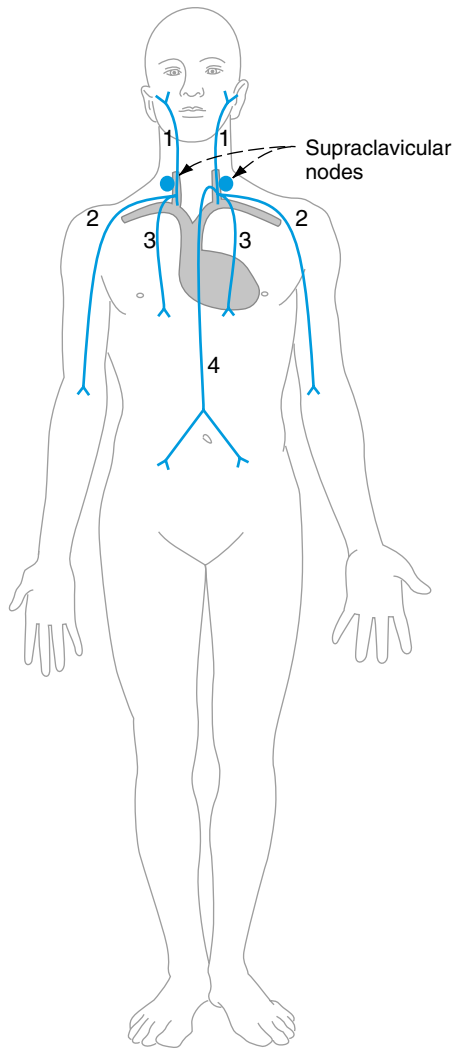


FIG. 27.1 THE SEVEN REGIONS OF LYMPHATIC DRAINAGE. All lymphatic drainage of the body converges on the right and left junctions of the internal jugular and subclavian veins (shaded gray, along with the superior vena cava and heart). The great veins on the right side of the neck receive drainage from: the right head and neck (region 1, traversing cervical nodes); the right arm, chest wall, and breast (region 2, traversing axillary nodes); and the right lung and mediastinal structures (region 3, via mediastinal and tracheobronchial nodes but no peripheral nodes). The left great veins receive drainage from similar regions of the left upper body (regions 1 to 3) and, via the thoracic duct, drainage from all tissues below the diaphragm (region 4). Only the supraclavicular nodes are depicted, illustrating their strategic proximity to the confluence of these seven major lymph channels.

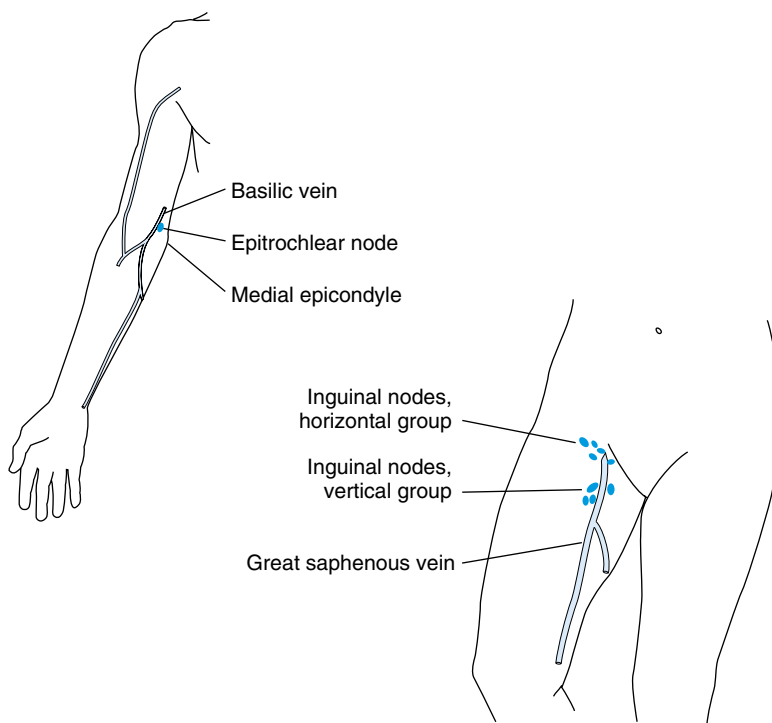


FIG. 27.2 EPITROCHLEAR AND INGUINAL NODES. The epitrochlear nodes (left side of figure) are located 2 to 3 cm above the medial epicondyle of the humerus, just medial to the basilic vein, which lies along the groove medial to the biceps muscle. The inguinal nodes (right side of figure) consist of a horizontal group and vertical group; the vertical group lies along the termination of the greater saphenous vein.

2. SUPRACLAVICULAR NODES

Although supraclavicular nodes actually belong to the deep cervical nodes, they are considered separately because of their strategic location in the base of the neck, close to where all lymph drainage returns to the systemic venous system (see Fig. 27.1). Because of this location, supraclavicular adenopathy may signify serious disease located in the thoracic or abdominal cavities, regions where nodes are otherwise hidden from the examiner. The anatomy depicted in Fig. 27.1 predicts that right supraclavicular adenopathy would be associated with disorders of the right thorax, arm, and neck and that the left supraclavicular adenopathy would be associated with disorders of the left thorax, arm, neck, and the abdomen and pelvis.

Normally, lymph flows from supraclavicular nodes downward toward the confluence of lymph channels and great veins (see Fig. 27.1). Therefore for intra-abdominal or intrathoracic disorders to involve the supraclavicular nodes, disease must spread in a *retrograde* direction from the thoracic duct or bronchomediastinal lymphatic vessels through the cervical efferents leaving the supraclavicular nodes. Such retrograde spread easily occurs and does not imply obstruction of lymphatic channels. In one investigation of 92 patients

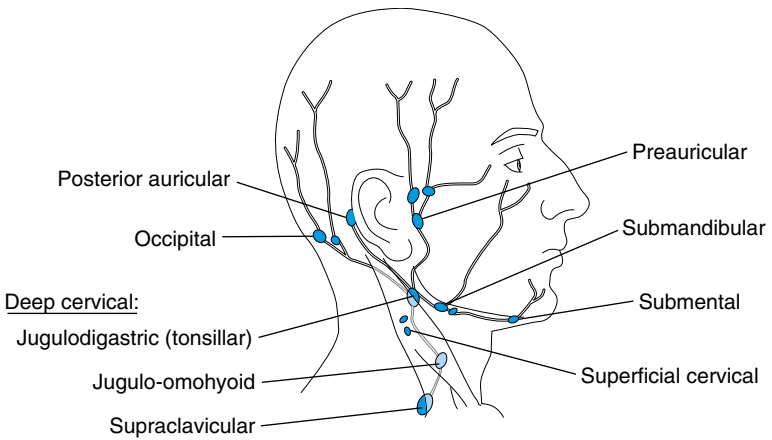


FIG. 27.3 CERVICAL LYMPH NODES. Superficial cervical nodes are named according to regional anatomy: occipital nodes, posterior auricular (or mastoid) nodes, preauricular (or parotid) nodes, submandibular nodes, submental nodes, and superficial cervical nodes. Deep cervical nodes lie along the carotid sheath and are mostly buried under the sternocleidomastoid muscle, although the uppermost nodes appear in front of this muscle and the lowermost posterior to it. Three deep cervical nodes have specific names because of their size and clinical importance: (1) the jugulodigastric node, an upper deep cervical node at the level of the hyoid bone that becomes tender and prominent in patients with pharyngitis (i.e., the tonsillar node), (2) the jugulo-omohyoid node, a lower deep cervical node located where the omohyoid muscle crosses the jugular vein (this node drains the tongue and may become enlarged in patients with tongue carcinoma), and (3) the supraclavicular nodes, which are the lowermost deep cervical nodes and are considered separately in the section on supraclavicular nodes.

undergoing lymphangiography of the lower limbs, radiopaque material appeared in the supraclavicular nodes within 48 hours in 55% of the patients.¹⁵ As expected, the dye opacified exclusively the left supraclavicular nodes in 48 of 51 patients, but it opacified both right and left supraclavicular nodes in two patients and exclusively the right supraclavicular nodes in one patient, indicating normal anatomic variation in the connections between the thoracic duct and supraclavicular nodes.¹⁵

Supraclavicular adenopathy appears just behind the clavicle, underneath or posterior to the sternocleidomastoid muscle. A Valsalva maneuver may make these nodes more prominent by pushing the apical pleural surface upward against the nodes and bringing them into view.¹⁶ In 1848 Virchow first observed the association between abdominal malignancies and metastases to supraclavicular nodes.^{15,17,18} Unaware of Virchow's description, the French clinician and pathologist Trosier described the same association in 1886, emphasizing the predisposition to the left side.^{15,17,18} Left supraclavicular adenopathy has been therefore called Virchow nodes, Trosier nodes, Virchow-Trosier nodes, sentinel nodes, or signal nodes.¹⁹

3. EPITROCHLEAR NODES

Epitrochlear nodes (supratrochlear or cubital nodes; see Fig. 27.2) are superficial nodes, located on the anteromedial arm 2 to 3 cm above the medial epicondyle of the humerus. They drain the ulnar side of the forearm and hand (i.e., little and ring fingers) and send efferents to the axillary nodes. A common

method for palpating these nodes is for the clinician to face the patient and reach across to shake the patient's hand on the side to be examined. The examiner then places his or her free hand behind the patient's arm, just proximal to the elbow, and uses his fingertips to palpate these nodes above and anterior to the medial epicondyle.

Although epitrochlear adenopathy may indicate infection or malignancy on the ulnar side of the forearm or hand, these nodes have historically been associated with conditions causing generalized lymphadenopathy, especially when they are enlarged bilaterally (see the sections on [Epitrochlear Adenopathy](#) and [Detecting HIV Infection in Developing Nations](#)). One hundred years ago epitrochlear adenopathy was felt to be a compelling sign of secondary syphilis, occurring in 25% to 93% of cases.²⁰⁻²² However, modern examples of this specific association are scarce.

4. AXILLARY NODES

Axillary nodes drain the ipsilateral arm, breast, and chest wall ([Fig. 27.4](#)). To examine these nodes, the clinician should ensure that the patient's axillary skin is relaxed, by first supporting and adducting the patient's arm. Nodes are located in the posterior, anterior, or medial walls of the axillary fossa or in its apex. Efferent lymph vessels travel directly to the systemic veins at the root of the neck, although a few efferents pass first through the ipsilateral supraclavicular nodes (see [Fig. 27.4](#)).^{9,11}

5. INGUINAL NODES

Inguinal nodes are superficial nodes that are organized into two groups: a proximal or *horizontal* group located just below the inguinal ligament, which drains the external genitalia, perineum, and lower anterior abdominal, and a distal or *vertical* group located at the termination of the great saphenous vein, which drains the leg (see [Fig. 27.2](#)).⁹

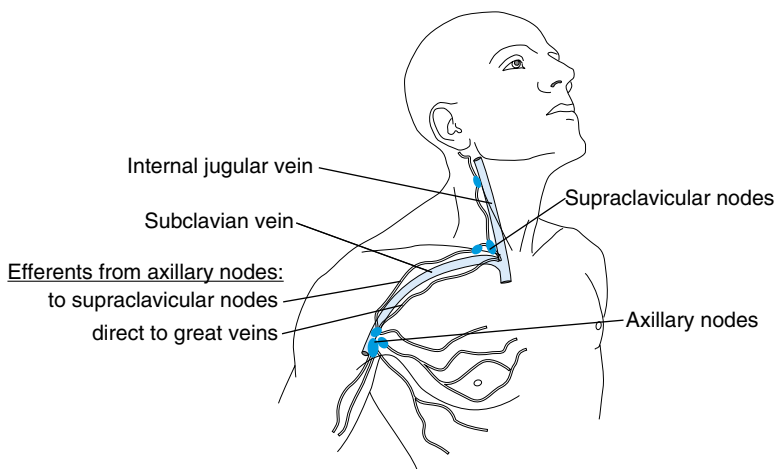


FIG. 27.4 AXILLARY NODES. The axillary nodes receive lymphatic drainage from the ipsilateral arm, breast, and chest wall. Efferent vessels travel to the great veins at the root of the neck, although a few vessels travel first through the supraclavicular nodal group.

III. THE FINDING

A. DESCRIBING ADENOPATHY

Important features to observe when describing adenopathy are location, size, number, hardness, and tenderness. *Fixed nodes* are immobile from attachments to adjacent structures, implying malignant invasion of these tissues. A *hard node* has the consistency of a rock, again implying malignant disease (the hardness presumably reflects the accompanying fibrosis induced by the tumor). *Shotty adenopathy* indicates multiple tiny superficial nodes, mimicking the sensation of buckshot under the skin, a finding sometimes observed in the inguinal region but without particular diagnostic significance.²³ The size of a particular node can be indicated by recording its maximal length and width or, as some investigators suggest, by recording the product of these two numbers (e.g., a node measuring 2.5 cm × 3 cm is “7.5 cm²”).

B. GENERALIZED LYMPHADENOPATHY

Generalized adenopathy is defined as simultaneous enlargement of two or more regional lymph node groups.²⁴ Most affected patients have either combined cervical and inguinal adenopathy or combined cervical and axillary adenopathy.²⁵ Generalized lymphadenopathy implies a systemic disorder affecting lymph nodes, such as lymphoma or leukemia, specific infectious diseases (e.g., infectious mononucleosis, HIV infection, or syphilis), anticonvulsant hypersensitivity syndrome, sarcoidosis, or connective tissue disorders.²⁴

C. “GLANDULAR” SYNDROMES

The term *glandular* refers to lymph nodes (e.g., *glandular fever* was the original name for infectious mononucleosis). Therefore the **ulceroglandular syndrome** is the triad of fever, ulceration on the distal arm or leg (indicating the portal of entry of infectious agent), and regional adenopathy. The **oculoglandular syndrome** (Parinaud syndrome*) describes the association of conjunctivitis with ipsilateral preauricular and submandibular adenopathy. Both ulceroglandular and oculoglandular syndromes have been associated with specific microbial agents (see the sections on **Ulceroglandular and Oculoglandular Syndromes**).

Chapter 25 reviews the Delphian node and Chapter 50 discusses the Sister Mary Joseph nodule.

IV. CLINICAL SIGNIFICANCE

A. DEFINITION OF DISEASE

EBM Box 27.1 reviews the diagnostic accuracy of physical examination in distinguishing serious causes of adenopathy from more benign disorders. All of the patients in these studies were referred to specialists because of persistent unexplained peripheral lymphadenopathy. Most patients (35% to 83%) presented with cervical adenopathy, 1% to 29% with supraclavicular adenopathy, 4% to 24% with axillary adenopathy, 3% to 16% with inguinal adenopathy, and 16% to 32% with generalized adenopathy.^{4,6,8,25,27,31,32}

* Henri Parinaud, one of the world's first neuro-ophthalmologists, was recruited to Paris by Charcot in the late 1800s. He also described the pupillary and eye movement abnormalities of the pretectal syndrome (see Chapter 21).²⁶

The etiology of lymphadenopathy in these studies was determined either by fine needle or excisional biopsy or, in a few low-risk patients who did not undergo biopsy, prolonged periods of observation.^{7,8} Some of these studies defined a “serious disorder” (or “disease”) as any disorder in which the biopsy results would imply specific treatment or prognosis. These studies therefore included both malignancy and granulomatous disease (e.g., tuberculosis or sarcoidosis) as “disease.”^{6,7,29-31,34,35} Other studies confined “disease” to the diagnosis of malignancy alone.^{8,27,28,32,33} Both definitions of disease are combined in [EBM Box 27.1](#) because analyzing the definitions separately revealed similar diagnostic accuracy and because the overwhelming majority of patients in all studies had a malignant cause for their disease.

B. EXTRANODAL MIMICS OF LYMPH NODES

Up to 15% of patients referred for unexplained “lymphadenopathy” instead have extranodal explanations for their subcutaneous lumps.⁸ Common mimics of lymphadenopathy at all locations are skin nodules, such as lipomas or epidermoid cysts. In the cervical region, thyroglossal cysts, branchial cleft cysts, and prominent carotid sinuses may be mistaken for nodes (see [Chapter 25](#)). In the supraclavicular region, synovial cysts from rheumatoid arthritis of the shoulder,³⁶ cervical ribs, and abnormal articulations of the first rib^{37,38} have all been mistaken for nodes.

C. INDIVIDUAL FINDINGS

In these studies the symptom of generalized pruritus argued for a serious cause, probably because of its association with lymphoma (sensitivity = 6% to 10%, specificity = 98% to 100%, likelihood ratio [LR] = 4.9).^{6,7} According to the LRs in [EBM Box 27.1](#), several physical findings also argue for serious disease: fixed lymph nodes (LR = 10.9), size of 9 cm² or more (i.e., the equivalent of 3 × 3 cm² or larger; LR = 8.4), weight loss (LR = 3.4), hard texture (LR = 3.2), supraclavicular adenopathy (LR = 3.2), and age of 40 years or more (LR = 2.4).

Only three findings argue against serious disease, all of them reducing probability only modestly: age less than 40 years (LR = 0.4), lymph node size less than 4 cm² (i.e., 2 × 2 cm² or smaller; LR = 0.4), and lymph node tenderness (LR = 0.4). Tenderness may be less specific for benign disorders than expected because hemorrhage or necrosis into neoplastic nodes also causes discomfort mimicking acute inflammatory changes. The symptom of throat soreness also argues against serious disease (sensitivity = 3% to 14%, specificity = 23% to 89%, LR = 0.2).^{6,7,35}

Findings that are unhelpful in distinguishing serious from benign disease include rash, regional distribution of nodes (other than supraclavicular location), fever, a palpable spleen, and a palpable liver (all LRs either not significant or very close to the value of 1).

The finding of generalized adenopathy, defined as involvement of two or more regional node groups, also lacks diagnostic value (LR not significant). Even when generalized lymphadenopathy is defined as involvement of four or more regional lymph node groups, it fails to discriminate serious from benign causes (LR not significant),³⁴ probably because this finding appears just as often in benign disorders (e.g., infectious mononucleosis) as in serious disorders (e.g., lymphoma).

D. COMBINED FINDINGS

Based on evaluation of more than 300 patients, Vassilakopoulos and others have identified six independent predictors of serious disease, creating a *lymph node score* that can easily be calculated at the bedside ([Table 27.1](#)).⁷ According to this scoring scheme, a score of −3 or less virtually excludes serious disease (LR = 0.04; see [EBM Box 27.1](#)), one of −2 or −1 argues against a serious cause (LR = 0.1), one

**EBM BOX 27.1****Lymphadenopathy***

Finding (Reference) [†]	Sensitivity (%)	Specificity (%)	Likelihood Ratio [‡] if Finding Is	
			Present	Absent
General and Skin Findings				
Male sex ^{6,7,27-29}	44-59	49-72	1.3	0.8
Age ≥40 years ^{6,7,27,28,30,31}	48-91	53-87	2.4	0.4
Weight loss ^{6,7,28,32}	19-28	90-95	3.4	0.8
Fever ^{6,7,29,32}	1-31	60-80	NS	NS
Distribution of Adenopathy				
Head and neck nodes (ex- cluding supraclavicular nodes) ^{6-8,27-29,31-33}	21-79	15-69	NS	NS
Supraclavicular nodes ^{6-8,28,31-33}	8-61	84-98	3.2	0.8
Axillary nodes ^{6-8,27-29,31-33}	8-52	30-91	0.8	NS
Inguinal nodes ^{6-8,27-29,31-33}	3-22	61-96	0.6	NS
Epitrochlear nodes ²⁹	2	97	NS	NS
Generalized lymphad- enopathy ^{8,27,34}	32-48	31-87	NS	NS
Characteristics of Adenopathy				
Lymph node size ^{6,7}				
<4 cm ²	33-36	9-37	0.4	—
4-8.99 cm ²	26-30	—	NS	—
≥9 cm ²	37-38	91-98	8.4	—
Hard texture ^{6,7}	48-62	83-84	3.2	0.6
Lymph node tender- ness ^{6,7,29,32}	3-18	50-86	0.4	1.3
Fixed lymph nodes ^{6,32}	12-56	97	10.9	NS
Other Findings				
Rash ^{7,29}	4-8	85-95	NS	NS
Palpable spleen ^{6,7,29}	5-10	92-96	NS	NS
Palpable liver ^{7,29}	14-16	86-89	NS	NS
Lymph Node Score^{6,7}				
-3 or less	1-3	42-72	0.04	—
-2 or -1	1-3	—	0.1	—
0 to 4	23	—	NS	—
5 or 6	17-26	—	5.1	—
7 or more	49-56	94-99	21.9	—

*Diagnostic standard: for diagnosis, see the text.

†Definition of findings: for finding, see the text.

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.

NS, Not significant.

[Click here to access calculator](#)

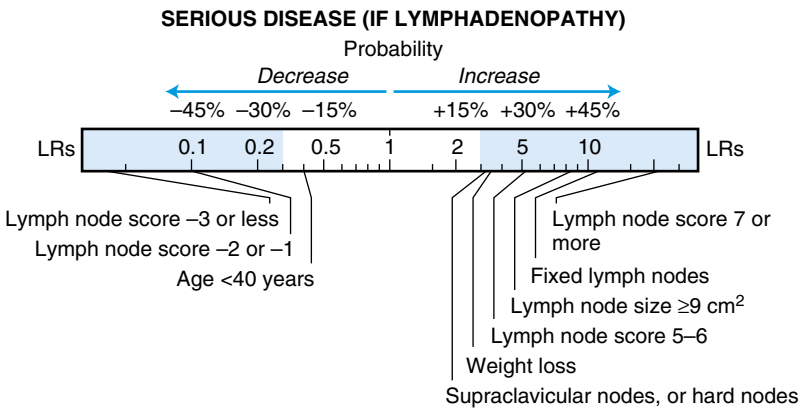


TABLE 27.1 Lymph Node Score*	
Finding	Points
Age >40 years	+5
Lymph node tenderness	-5
Lymph node size	
<1 cm ²	0
1-3.99 cm ²	+4
4-8.99 cm ²	+8
≥9 cm ²	+12
Generalized pruritus	+4
Supraclavicular nodes present	+3
Lymph node is hard	+2
Correction factor	-6†

*Based on reference 7.

†Included in every patient's score. For example, a 55-year-old asymptomatic patient with nontender but hard supraclavicular adenopathy measuring 6 cm² has a score of 12 (i.e., 5 + 8 + 3 + 2 - 6).

of 5 or 6 argues for a serious disorder (LR = 5.1), and one of 7 or more is practically diagnostic for serious disease (LR = 21.9). Scores of 0 to 4 lack diagnostic significance.

E. LYMPH NODE SYNDROMES
I. SUPRACLAVICULAR ADENOPATHY

In studies confined to patients undergoing biopsy of supraclavicular adenopathy, 54% to 87% of patients are discovered to have malignancy, mostly metastatic carcinoma (46% to 69% of all patients).³⁸⁻⁴⁴ As expected, supradiaphragmatic carcinomas (e.g., lung or breast carcinoma) are equally distributed between the right and left sides. Most lung and breast cancers spread to the ipsilateral supraclavicular nodes, although examples of contralateral spread occur.^{11,18,39-44}

Surprisingly, infradiaphragmatic carcinomas do not always spread to the left supraclavicular nodes as would be predicted by normal anatomy (see Fig. 27.1)

and implied by Virchow's and Trosier's eponym. On average, only three-quarters of infradiaphragmatic carcinomas metastatic to supraclavicular nodes go to the left side; one-quarter appear on the *right* side (range = 0% to 38%). Two proposed mechanisms for involvement of the right side by these tumors include the following: (1) some patients normally have anatomic connections between the thoracic duct and the right supraclavicular nodes (see the section on [Supraclavicular Nodes](#)), and (2) metastatic tumor first involves the mediastinal nodes, which via the right broncho-mediastinal lymphatic vessels provide passage to the right neck. In support of the second explanation, one autopsy study of patients with infradiaphragmatic malignancies metastatic to the supraclavicular nodes documented that most patients also had mediastinal metastases.¹⁸

Approximately 50% of patients whose supraclavicular node biopsies revealed malignancy were unaware of the diagnosis before biopsy,^{18,41} illustrating the diagnostic importance of this node. In patients with metastases to the *right* supraclavicular node, the most common primary tumors by far are lung and breast cancer, followed by esophageal cancer and a medley of other tumors located above and below the diaphragm.^{18,39-44} In those with metastases to the *left* side, lung, breast, gastric, and gynecologic primary tumors figure prominently in reported series of cases, although carcinoma of virtually any organ located in the thorax, abdomen, and pelvis has been associated with metastases to these nodes.^{18,39-47}

2. EPITROCHLEAR ADENOPATHY

Epitrochlear nodes are a rare finding in normal individuals but are commonly observed in patients with disorders causing generalized lymphadenopathy. They are palpable in 25% to 30% of patients with sarcoidosis, lymphoma, and chronic lymphocytic leukemia and up to 55% of patients with infectious mononucleosis.²⁰

3. IDENTIFYING HUMAN IMMUNODEFICIENCY VIRUS INFECTION IN DEVELOPING NATIONS

Adenopathy provides an important clue to HIV infection in patients from developing nations. In one study of hospitalized patients in Zimbabwe, where HIV infection is prevalent, the finding of epitrochlear adenopathy (i.e., epitrochlear nodes >0.5 cm diameter) distinguished patients with HIV seropositivity from those without it (sensitivity = 84%, specificity = 81%, positive LR = 4.5, negative LR = 0.2).⁴⁸ In studies from both Zimbabwe and India the finding of axillary adenopathy in patients being treated for active tuberculosis detects HIV coinfection (sensitivity = 26% to 43%, specificity = 93% to 95%, positive LR = 4.9).^{48,49}

4. FEVER OF UNKNOWN ORIGIN

The finding of peripheral lymphadenopathy in a patient with fever of unknown origin is a modest indicator that a bone marrow examination will be diagnostic (usually of a hematologic malignancy; LR = 1.9; see [Chapter 18](#) and section on Fever of Unknown Origin).⁵⁰⁻⁵²

5. STAGING PATIENTS WITH KNOWN CANCER

The absence of regional adenopathy is often unhelpful when staging patients with known malignancies. For example, up to 50% of patients with head and neck tumors and negative nodes by examination have nodal metastases discovered during radical neck exploration.⁵³⁻⁵⁵ In women with breast carcinoma, palpable axillary adenopathy does indicate metastatic nodal disease (sensitivity = 31% to 35%, specificity = 94% to 98%, positive LR = 9.3), but the absence of adenopathy is unhelpful (negative LR = 0.7), and 18% to 33% of patients with negative axillary examinations

have axillary nodal metastases discovered at surgery.^{56,57} Finally, up to one-quarter of patients with lung carcinoma and negative supraclavicular nodes have involvement of these nodes histologically.^{58,59} Bedside examination is inaccurate because malignancy may involve regional nodes without changing their appearance. Even surgeons directly inspecting the physical characteristics of dissected nodes during staging operations often cannot distinguish metastatic nodes from normal ones.^{53,55}

6. ULCEROGLANDULAR AND OCULOGLANDULAR SYNDROMES

Common reported causes of the ulceroglandular syndrome are tularemia, rickettsial infections, and herpes simplex infections.⁶⁰ Important etiologies of the oculoglandular syndrome are cat-scratch disease, tularemia, and viral infections (especially enterovirus and adenovirus).⁶¹

The references for this chapter can be found on www.expertconsult.com.

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